Medical Policy
Genetic Testing for Rett Syndrome

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Policy Number: 803
BCBSA Reference Number: 2.04.81

Related Policies
None

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Mutation testing for Rett syndrome may be considered MEDICALLY NECESSARY to confirm a diagnosis of Rett syndrome in a female child with developmental delay and signs/symptoms of Rett syndrome, but when there is uncertainty in the clinical diagnosis.

All other indications for mutation testing for Rett syndrome, including prenatal screening and testing of family members, are considered INVESTIGATIONAL.

Prior Authorization Information
Commercial Members: Managed Care (HMO and POS)
Prior authorization is NOT required.

Commercial Members: PPO, and Indemnity
Prior authorization is NOT required.

Medicare Members: HMO Blue℠
Prior authorization is NOT required.

Medicare Members: PPO Blue℠
Prior authorization is NOT required.

CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an
individual member. A draft of future ICD-10 Coding related to this document, as it might look today, is included below for your reference.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

<table>
<thead>
<tr>
<th>CPT codes</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81302</td>
<td>MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81303</td>
<td>MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; known familial variant</td>
</tr>
<tr>
<td>81304</td>
<td>MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; duplication/deletion variants</td>
</tr>
</tbody>
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ICD-9 Diagnosis Codes

<table>
<thead>
<tr>
<th>ICD-9 codes</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>330.8</td>
<td>Rett’s syndrome</td>
</tr>
<tr>
<td>330.9</td>
<td>Unspecified cerebral degeneration in childhood</td>
</tr>
<tr>
<td>783.40</td>
<td>Lack of expected normal physiological development in childhood</td>
</tr>
</tbody>
</table>

ICD-10-CM Diagnosis Codes

<table>
<thead>
<tr>
<th>ICD-10-CM codes</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F84.2</td>
<td>Rett's syndrome</td>
</tr>
<tr>
<td>G94</td>
<td>Other disorders of brain in diseases classified elsewhere</td>
</tr>
<tr>
<td>R62.50</td>
<td>Unspecified lack of expected normal physiological development in childhood</td>
</tr>
<tr>
<td>R62.59</td>
<td>Other lack of expected normal physiological development in childhood</td>
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</table>

Description

Rett syndrome (RTT), a neurodevelopmental disorder, is usually caused by mutations in the MECP2 gene. Genetic testing is available to determine whether a pathogenic mutation exists in a patient with clinical features of Rett syndrome, or in a patient's family member.

RTT is characterized by apparent normal development for the first 6-18 months of life, followed by the loss of intellectual functioning, loss of acquired fine and gross motor skills and the ability to engage in social interaction. There is wide variability in the rate of progression and severity of the disease. The diagnosis of RTT remains a clinical one, using diagnostic clinical criteria that have been established for the diagnosis of classic and variant Rett syndrome.

Approximately 99.5% of cases of RTT are sporadic, resulting from a de novo mutation, which arise almost exclusively on the paternally derived X chromosome. The percent of total cases, 0.5% of cases, are familial and usually explained by germline mosaicism or favorably skewed X-chromosome inactivation in the carrier mother that results in her being unaffected or only slightly affected (mild mental retardation). In the case of a carrier mother, the recurrence risk of RTT is 50%.

The identification of a mutation in MECP2 does not necessarily equate to a diagnosis of RTT. A proportion of patients with a clinical diagnosis of RTT do not appear to have mutations in the MECP2 gene. Two other genes, CDKL5 and Netrin G, have been shown to be associated with a phenotype that strongly overlaps that seen in RTT.
Summary
MECP2 mutations are found in the majority of patients with RTT, particularly those who present with classical clinical features of RTT. The diagnostic accuracy of mutation testing for RTT cannot be determined with absolute certainty given the lack of a true gold standard for the diagnosis of RTT, but appears to have high sensitivity and specificity.

Testing for MECP2 mutations has clinical utility in certain clinical scenarios. Although there is no effective treatment for RTT, and management is mainly supportive, a definitive diagnosis can end a diagnostic workup for other possible diagnoses and may alter some aspects of management (e.g., determining whether or not to advise avoidance of medications that can prolong QT interval). Testing of family members and prenatal testing in a couple who have had a child with RTT or mental retardation due to a MECP2 mutation is not likely to improve outcomes. The risk of a family having a second child with the disorder is less than 1 percent, except in the rare situation where the mother carries the mutation, and the impact on decision making on health outcomes is uncertain.

Therefore, mutation testing for Rett syndrome may be considered medically necessary to confirm a diagnosis of Rett syndrome in a female child with developmental delay and signs/symptoms of Rett syndrome when there is uncertainty in the clinical diagnosis; however, all other indications for mutation testing for Rett syndrome, including prenatal screening and testing of family members, are considered investigational.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>6/2014</td>
<td>Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.</td>
</tr>
<tr>
<td>12/2013</td>
<td>New references from BCBSA National medical policy.</td>
</tr>
<tr>
<td>2/2013</td>
<td>New policy describing coverage and non-coverage</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References


